APPROVED BY DRAFTSMAN
RECLASS

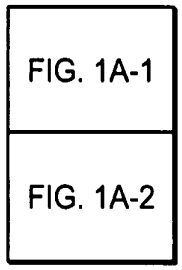


FIG. 1A

```
GAATTCCCCCAACAGAGCCAAGCTCTCCATCTAGTGGACAGGGAAGCTAGCAGCAAACC      39 (UPPER: SEQ ID NO.: 1)
                                                                  19 (LOWER: SEQ ID NO.: 4)

TTCCCTTCACTACAAAACTTCATTGCTTGGCCAAAAAGAGAGTTAATTCAATGTAGACAT     119
                                                                  39

CTATGTAGGCAATTAAAAACCTATTGATGTATAAAACAGTTTGCATTCATGGAGGGCAAC     179
                                                                  59

TAAATACATTCTAGGACTTTATAAAAGATCACTTTTTATTTATGCACAGGGTGGAACAAG     239
                                                                  79

ATGGATTATCAAGTGTCAAGTCCAATCTATGACATCAATTATTATACATCGGAGCCCTGC     299
 M  D  Y  Q  V  S  S  P  I  Y  D  I  N  Y  Y  T  S  E  P  C      99
```

FIG. 1A-1

1/20

#4

```
CAAAAAATCAATGTGAAGCAAATCGCAGCCCGCCTCCTGCCTCCGCTCTACTCACTGGTG    359
 Q  K  I  N  V  K  Q  I  A  A  R  L  L  P  P  L  Y  S  L  V    119

TTCATCTTTGGTTTTGTGGGCAACATGCTGGTCATCCTCATCCTGATAAACTGCAAAAGG    419
 F  I  F  G  F  V  G  N  M  L  V  I  L  I  L  I  N  C  K  R    139

CTGAAGAGCATGACTGACATCTACCTGCTCAACCTGGCCATCTCTGACCTGTTTTTCCTT    479
 L  K  S  M  T  D  I  Y  L  L  N  L  A  I  S  D  L  F  F  L    159

CTTACTGTCCCCTTCTGGGCTCACTATGCTGCCGCCCAGTGGGACTTTGGAAATACAATG    539
 L  T  V  P  F  W  A  H  Y  A  A  A  Q  W  D  F  G  N  T  M    179

TGTCAACTCTTGACAGGGCTCTATTTTATAGGCTTCTTCTCTGGAATCTTCTTCATCATC    599
 C  Q  L  L  T  G  L  Y  F  I  G  F  F  S  G  I  F  F  I  I    199

CTCCTGACAATCGATAGGTACCTGGCTGTCGTCCATGCTGTGTTTGCTTTAAAAGCCAGG    659
 L  L  T  I  D  R  Y  L  A  V  V  H  A  V  F  A  L  K  A  R    219

ACGGTCACCTTTGGGGTGGTGACAAGTGTGATCACTTGGGTGGTGGCTGTGTTTGCGTCT    719
 T  V  T  F  G  V  V  T  S  V  I  T  W  V  V  A  V  F  A  S    239

CTCCCAGGAATCATCTTTACCAGATCTCAAAAAGAAGGTCTTCATTACACCTGCAGCTCT    779
 L  P  G  I  I  F  T  R  S  Q  K  E  G  L  H  Y  T  C  S  S    259

CATTTTCCATACA
 H  F  P  Y
```

FIG. 1A-2

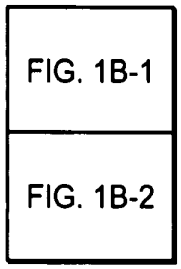


FIG. 1B

```
GAATTCCCCCAACAGAGCCAAGCTCTCCATCTAGTGGACAGGGAAGCTAGCAGCAAACC    59 (UPPER: SEQ ID NO.: 2)
                                                               19 (LOWER: SEQ ID NO.: 5)

TTCCCTTCACTACAAAACTTCATTGCTTGGCCAAAAAGAGAGTTAATTCAATGTAGACAT   119
                                                               39

CTATGTAGGCAATTAAAAACCTATTGATGTATAAAACAGTTTGCATTCATGGAGGGCAAC   179
                                                               59

TAAATACATTCTAGGACTTTATAAAAGATCACTTTTTATTTATGCACAGGGTGGAACAAG   239
                                                               79

ATGGATTATCAAGTGTCAAGTCCAATCTATGACATCAATTATTATACATCGGAGCCCTGC   299
 M  D  Y  Q  V  S  S  P  I  Y  D  I  N  Y  Y  T  S  E  P  C    99
```

FIG. 1B-1

```
CAAAAAATCAATGTGAAGCAAATCGCAGCCCGCCTCCTGCCTCCGCTCTACTCACTGGTG   359
 Q  K  I  N  V  K  Q  I  A  A  R  L  L  P  P  L  Y  S  L  V   119

TTCATCTTTGGTTTTGTGGGCAACATGCTGGTCATCCTCATCCTGATAAACTGCAAAAGG   419
 F  I  F  G  F  V  G  N  M  L  V  I  L  I  L  I  N  C  K  R   139

CTGAAGAGCATGACTGACATCTACCTGCTCAACCTGGCCATCTCTGACCTGTTTTTCCTT   479
 L  K  S  M  T  D  I  Y  L  L  N  L  A  I  S  D  L  F  F  L   159

CTTACTGTCCCCTTCTGGGCTCACTATGCTGCCGCCCAGTGGGACTTTGGAAATACAATG   539
 L  T  V  P  F  W  A  H  Y  A  A  A  Q  W  D  F  G  N  T  M   179

TGTCAACTCTTGACAGGGCTCTATTTTATAGGCTTCTTCTCTGGAATCTTCTTCATCATC   599
 C  Q  L  L  T  G  L  Y  F  I  G  F  F  S  G  I  F  F  I  I   199

CTCCTGACAATCGATAGGTACCTGGCTGTCGTCCATGCTGTGTTTGCTTTAAAAGCCAGG   659
 L  L  T  I  D  R  Y  L  A  V  V  H  A  V  F  A  L  K  A  R   219

ACGGTCACCTTTGGGGTGGTGACAAGTGTGATCACTTGGGTGGTGGCTGTGTTTGCGTCT   719
 T  V  T  F  G  V  V  T  S  V  I  T  W  V  V  A  V  F  A  S   239

CTCCCAGGAATCATCTTTACCAGATCTCAAAAAGAAGGTCTTCATTACACCTGCAGCTCT   779
 L  P  G  I  I  F  T  R  S  Q  K  E  G  L  H  Y  T  C  S  S   259

CATTTTCCATACAGTCAGTATCAATTCTGGAAGAATTTCCAGACATTAAAGATAGTCATC   839
 H  F  P  Y  S  Q  Y  Q  F  W  K  N  F  Q  T  L  K  I  V  I   279
```

FIG. 1B-2

```
TTGGGGCTGGTCCTGCCGCTGCTTGTCATGGTCATCTGCTACTCGGGAATCCTAAAAACT    899
 L  G  L  V  L  P  L  L  V  M  V  I  C  Y  S  G  I  L  K  T    299

CTGCTTCGGTGTCGAAATGAGAAGAAGAGGCACAGGGCTGTGAGGCTTATCTTCACCATC    959
 L  L  R  C  R  N  E  K  K  R  H  R  A  V  R  L  I  F  T  I    319

ATGATTGTTTATTTTCTCTTCTGGGCTCCCTACAACATTGTCCTTCTCCTGAACACCTTC   1019
 M  I  V  Y  F  L  F  W  A  P  Y  N  I  V  L  L  L  N  T  F    339

CAGGAATTCTTTGGCCTGAATAATTGCAGTAGCTCTAACAGGTTGGACCAAGCTATGCAG   1079
 Q  E  F  F  G  L  N  N  C  S  S  S  N  R  L  D  Q  A  M  Q    359

GTGACAGAGACTCTTGGGATGACGCACTGCTGCATCAACCCCATCATCTATGCCTTTGTC   1139
 V  T  E  T  L  G  M  T  H  C  C  I  N  P  I  I  Y  A  F  V    379

GGGGAGAAGTTCAGAAACTACCTCTTAGTCTTCTTCCAAAAGCACATTGCCAAACGCTTC   1199
 G  E  K  F  R  N  Y  L  L  V  F  F  Q  K  H  I  A  K  R  F    399

TGCAAATGCTGTTCTATTTTCCAGCAAGAGGCTCCCGAGCGAGCAAGCTCAGTTTACACC   1259
 C  K  C  C  S  I  F  Q  Q  E  A  P  E  R  A  S  S  V  Y  T    419

CGATCCACTGGGGAGCAGGAAATATCTGTGGGCTTGTGACACGGACTCAAGTGGGCTGGT   1319
 R  S  T  G  E  Q  E  I  S  V  G  L  *                         439

GACCCAGTCAGAGTTGTGCACATGGCTTAGTTTTCATACACAGCCTGGGCTGGGGGTNGG   1379
                                                                459

TTGGNNGAGGTCTTTTTTAAAAGGAAGTTACTGTTATAGAGGGTCTAAGATTCATCCATT   1439
                                                                479

TATTTGGCATCTGTTTAAAGTAGATTAGATCCGAATTC
```

FIG. 1B-3

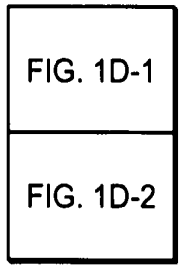


FIG. 1D

```
GAATTCCCCCAACAGAGCCAAGCTCTCCATCTAGTGGACAGGGAAGCTAGCAGCAAACC      59 (UPPER: SEQ ID NO. 3)
                                                                 19 (LOWER: SEQ ID NO. 6)

TTCCCTTCACTACAAAACTTCATTGCTTGGCCAAAAAGAGAGTTAATTCAATGTAGACAT     119
                                                                 39

CTATGTAGGCAATTAAAAACCTATTGATGTATAAAACAGTTTGCATTCATGGAGGGCAAC     179
                                                                 59

TAAATACATTCTAGGACTTTATAAAAGATCACTTTTTATTTATGCACAGGGTGGAACAAG     239
                                                                 79

ATGGATTATCAAGTGTCAAGTCCAATCTATGACATCAATTATTATACATCGGAGCCCTGC     299
 M  D  Y  Q  V  S  S  P  I  Y  D  I  N  Y  Y  T  S  E  P  C      99
```

FIG. 1D-1

```
CAAAAAATCAATGTGAAGCAAATCGCAGCCCGCCTCCTGCCTCCGCTCTACTCACTGGTG    359
 Q  K  I  N  V  K  Q  I  A  A  R  L  L  P  P  L  Y  S  L  V    119

TTCATCTTTGGTTTTGTGGGCAACATGCTGGTCATCCTCATCCTGATAAACTGCAAAAGG    419
 F  I  F  G  F  V  G  N  M  L  V  I  L  I  L  I  N  C  K  R    139

CTGAAGAGCATGACTGACATCTACCTGCTCAACCTGGCCATCTCTGACCTGTTTTTCCTT    479
 L  K  S  M  T  D  I  Y  L  L  N  L  A  I  S  D  L  F  F  L    159

CTTACTGTCCCCTTCTGGGCTCACTATGCTGCCGCCCAGTGGGACTTTGGAAATACAATG    539
 L  T  V  P  F  W  A  H  Y  A  A  A  Q  W  D  F  G  N  T  M    179

TGTCAACTCTTGACAGGGCTCTATTTTATAGGCTTCTTCTCTGGAATCTTCTTCATCATC    599
 C  Q  L  L  T  G  L  Y  F  I  G  F  F  S  G  I  F  F  I  I    199

CTCCTGACAATCGATAGGTACCTGGCTGTCGTCCATGCTGTGTTTGCTTTAAAAGCCAGG    659
 L  L  T  I  D  R  Y  L  A  V  V  H  A  V  F  A  L  K  A  R    219

ACGGTCACCTTTGGGGTGGTGACAAGTGTGATCACTTGGGTGGTGGCTGTGTTTGCGTCT    719
 T  V  T  F  G  V  V  T  S  V  I  T  W  V  V  A  V  F  A  S    239

CTCCCAGGAATCATCTTTACCAGATCTCAAAAAGAAGGTCTTCATTACACCTGCAGCTCT    779
 L  P  G  I  I  F  T  R  S  Q  K  E  G  L  H  Y  T  C  S  S    259

CATTTTCCATACATTAAAGATAGTCATCTTGGGGCTGGTCCTGCCGCTGCTTGTCATGGT    839
 H  F  P  Y  I  K  D  S  H  L  G  A  G  P  A  A  A  C  H  G    279
```

FIG. 1D-2

```
CATCTGCTACTCGGGAATCCTAAAAACTCTGCTTCGGTGTCGAAATGAGAAGAAGAGGCA    899
 H  L  L  L  G  N  P  K  N  S  A  S  V  S  K  *                 299

CAGGGCTGTGAGGCTTATCTTCACCATCATGATTGTTTATTTTCTCTTCTGGGCTCCCTA    959
                                                                 319

CAACATTGTCCTTCTCCTGAACACCTTCCAGGAATTCTTTGGCCTGAATAATTGCAGTAG    1019
                                                                 339

CTCTAACAGGTTGGACCAAGCTATGCAGGTGACAGAGACTCTTGGGATGACGCACTGCTG    1079
                                                                 359

CATCAACCCCATCATCTATGCCTTTGTCGGGGAGAAGTTCAGAAACTACCTCTTAGTCTT    1139
                                                                 379

CTTCCAAAAGCACATTGCCAAACGCTTCTGCAAATGCTGTTCTATTTTCCAGCAAGAGGC    1199
                                                                 399

TCCCGAGCGAGCAAGCTCAGTTTACACCCGATCCACTGGGGAGCAGGAAATATCTGTGGG    1259
                                                                 419

CTTGTGACACGGACTCAAGTGGGCTGGTGACCCAGTCAGAGTTGTGCACATGGCTTAGTT    1319
                                                                 439

TTCATACACAGCCTGGGCTGGGGGTNGGTTGGNNGAGGTCTTTTTTAAAAGGAAGTTACT    1379
                                                                 459

GTTATAGAGGGTCTAAGATTCATCCATTTATTTGGCATCTGTTTAAAGTAGATTAGATCC    1439
                                                                 479

GAATTC
```

FIG. 1D-3

FIG. 2A

FIG. 2B

FIG. 2

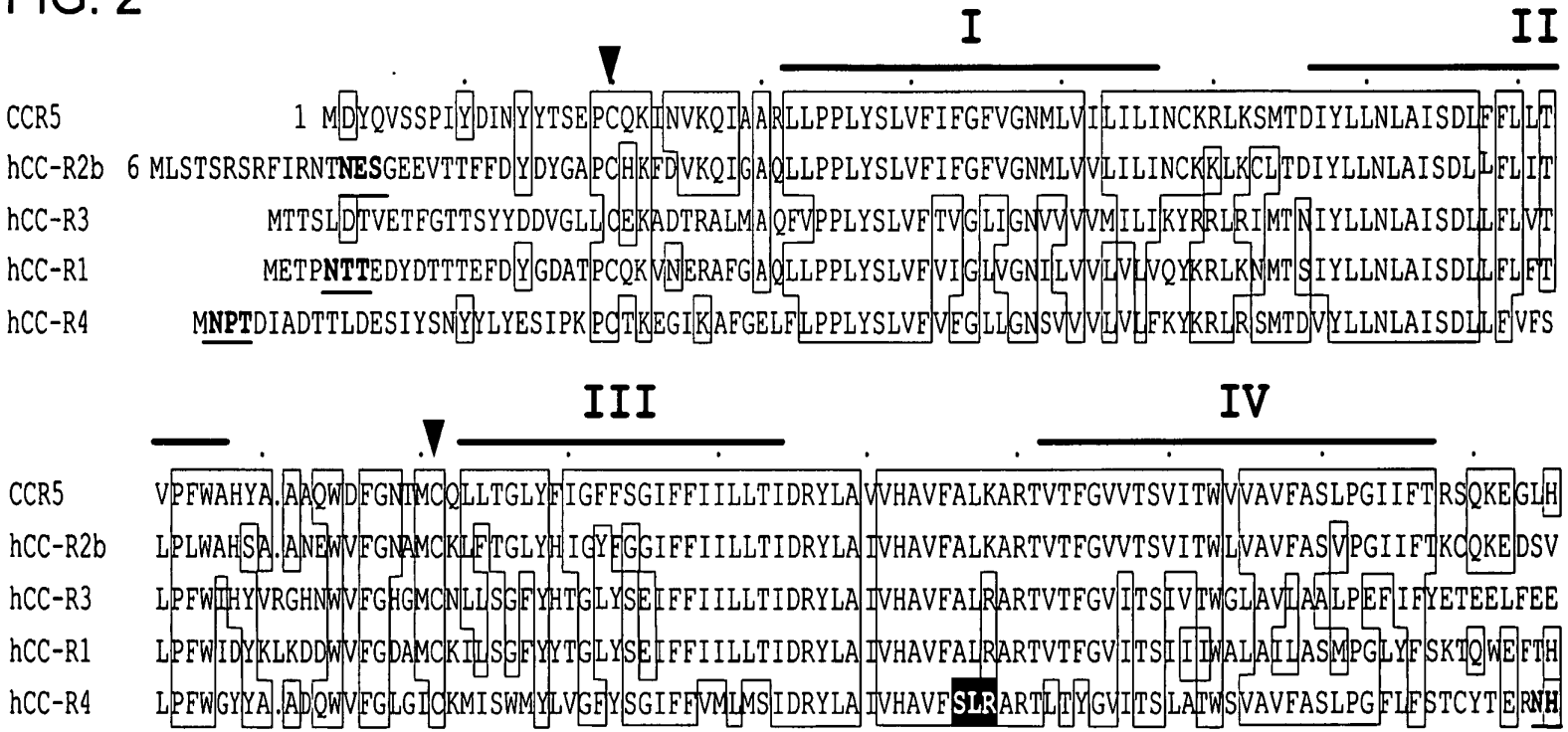


FIG. 2A

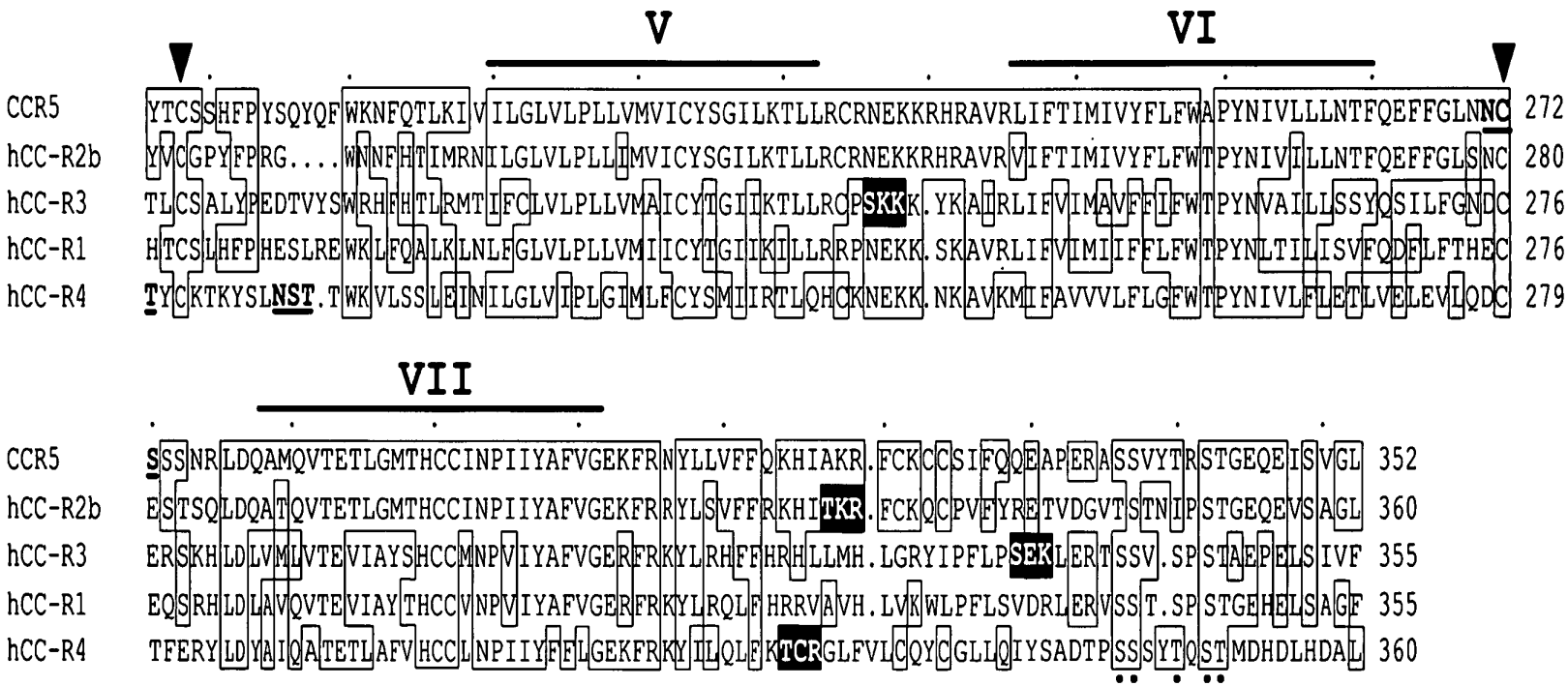

V
VI
VII
CCR5 YTCSSHFPYSQYQFWKNFQTLKIVILGLVLPLLVMVICYSGILKTLLRCRNEKKRHRAVRLIFTIMIVYFLFWAPYNIVLLLNTFQEFFGLNNC 272
hCC-R2b YVCGPYFPRG....WNNFHTIMRNILGLVLPLLIMVICYSGILKTLLRCRNEKKRHRAVRVIFTIMIVYFLFWTPYNIVILLNTFQEFFGLSNC 280
hCC-R3 TLCSALYPEDTVYSWRHFHTLRMTIFCLVLPLLVMAICYTGIIKTLLRCPSKKK.YKAIRLIFVIMAVFFIFWTPYNVAILLSSYQSILFGNDC 276
hCC-R1 HTCSLHFPHESLREWKLFQALKLNLFGLVLPLLVMIICYTGIIKILLRRPNEKK.SKAVRLIFVIMIIFFLFWTPYNLTILISVFQDFLFTHEC 276
hCC-R4 TYCKTKYSLNST.TWKVLSSLEINILGLVIPLGIMLFCYSMIIRTLQHCKNEKK.NKAVKMIFAVVVLFLGFWTPYNIVLFLETLVELEVLQDC 279
SSSNRLDQAMQVTETLGMTHCCINPIIYAFVGEKFRNYLLVFFQKHIAKR.FCKCCSIFQQEAPERASSVYTRSTGEQEISVGL 352
hCC-R2b ESTSQLDQATQVTETLGMTHCCINPIIYAFVGEKFRRYLSVFFRKHITKR.FCKQCPVFYRETVDGVTSTNTPSTGEQEVSAGL 360
hCC-R3 ERSKHLDLVMLVTEVIAYSHCCMNPVIYAFVGERFRKYLRHFFHRHLLMH.LGRYIPFLPSEKLERTSSV.SPSTAEPELSIVF 355
hCC-R1 EQSRHLDLAVQVTEVIAYTHCCVNPVIYAFVGERFRKYLRQLFHRRVAVH.LVKWLPFLSVDRLERVSST.SPSTGEHELSAGF 355
hCC-R4 TFERYLDYAIQATETLAFVHCCLNPIIYFFLGEKFRKYILQLFKTCRGLFVLCQYCGLLQIYSADTPSSSYTQSTMDHDLHDAL 360

FIG. 2B

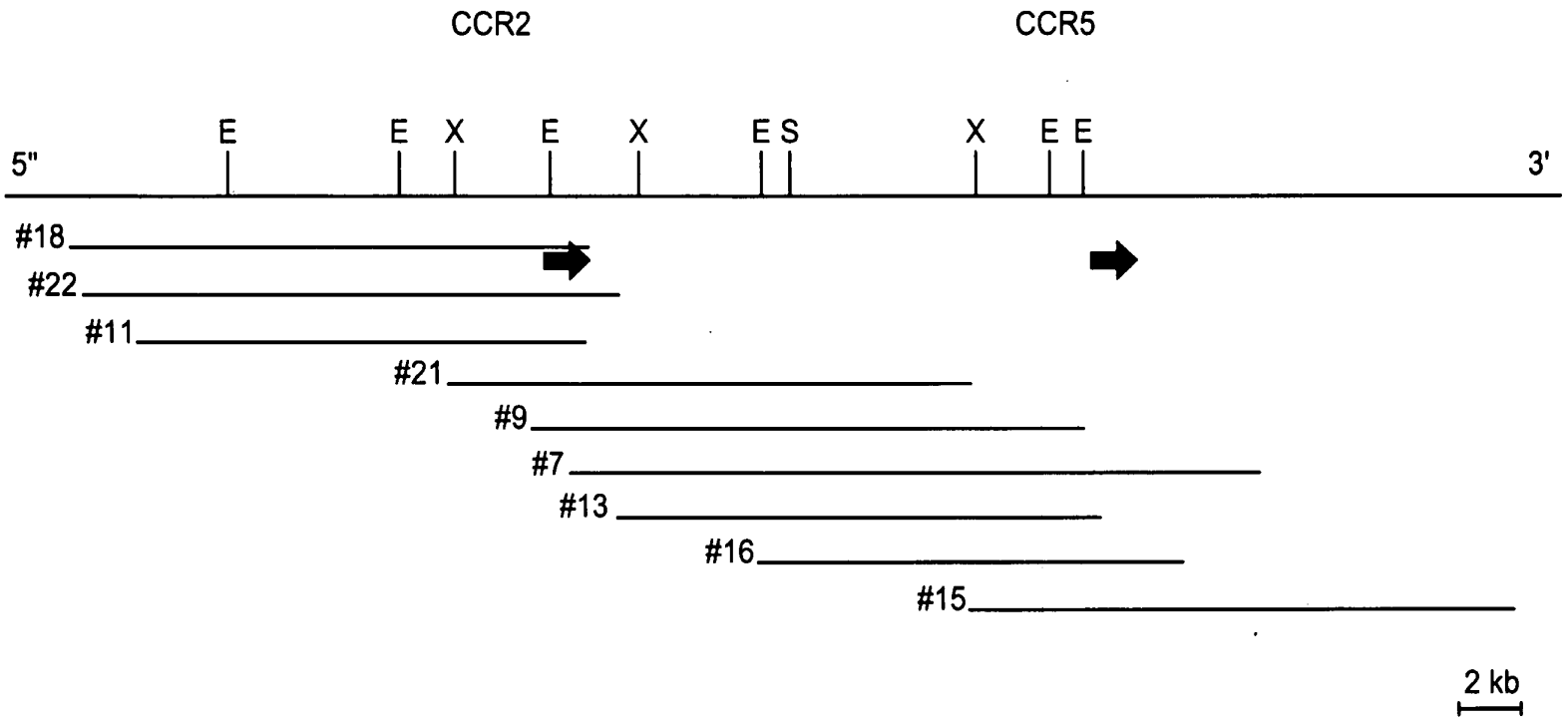


FIG. 3

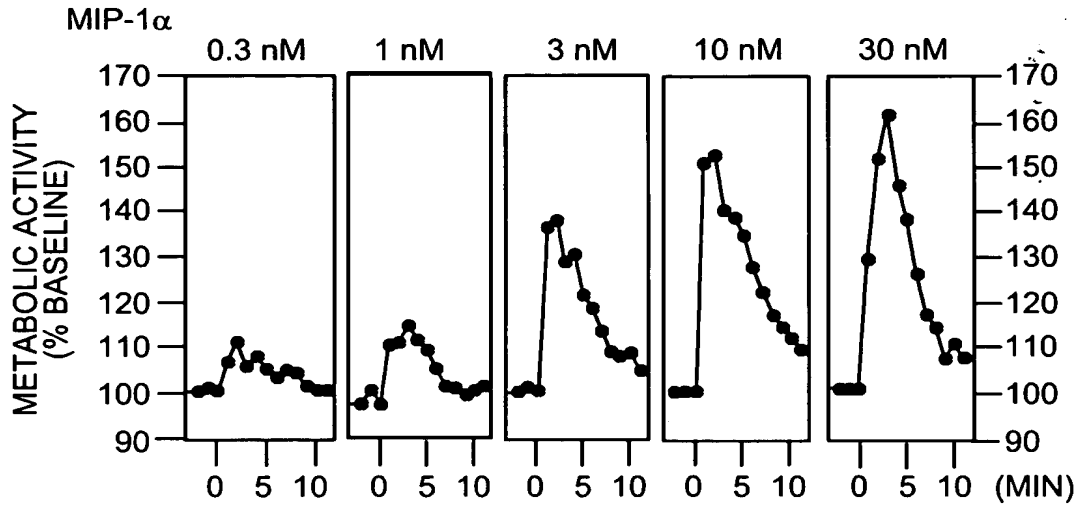

MIP-1α
0.3 nM
1 nM
3 nM
10 nM
30 nM
METABOLIC ACTIVITY
(% BASELINE)
170
160
150
140
130
120
110
100
90
0 5 10
(MIN)

FIG. 4A

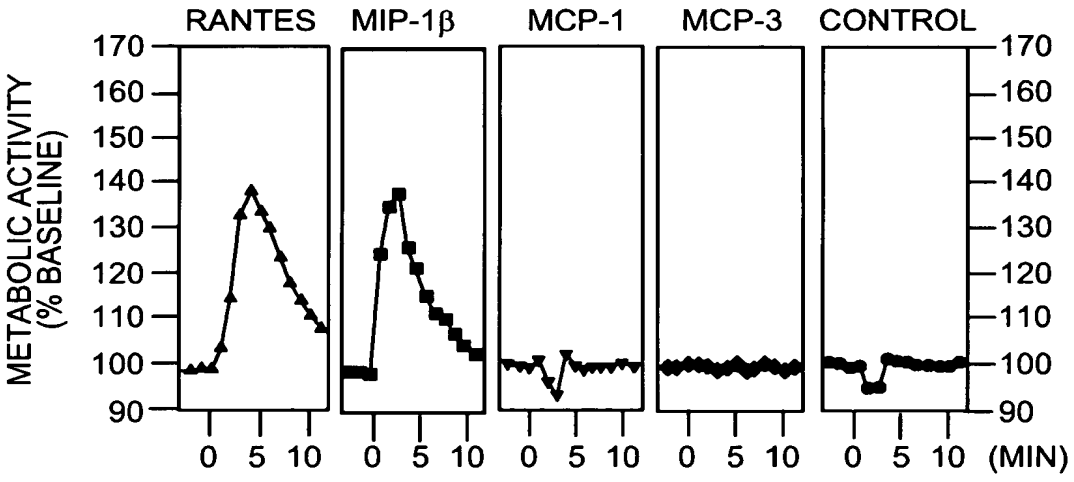

RANTES
MIP-1β
MCP-1
MCP-3
CONTROL
METABOLIC ACTIVITY
(% BASELINE)
170
160
150
140
130
120
110
100
90
0 5 10
(MIN)

FIG. 4B

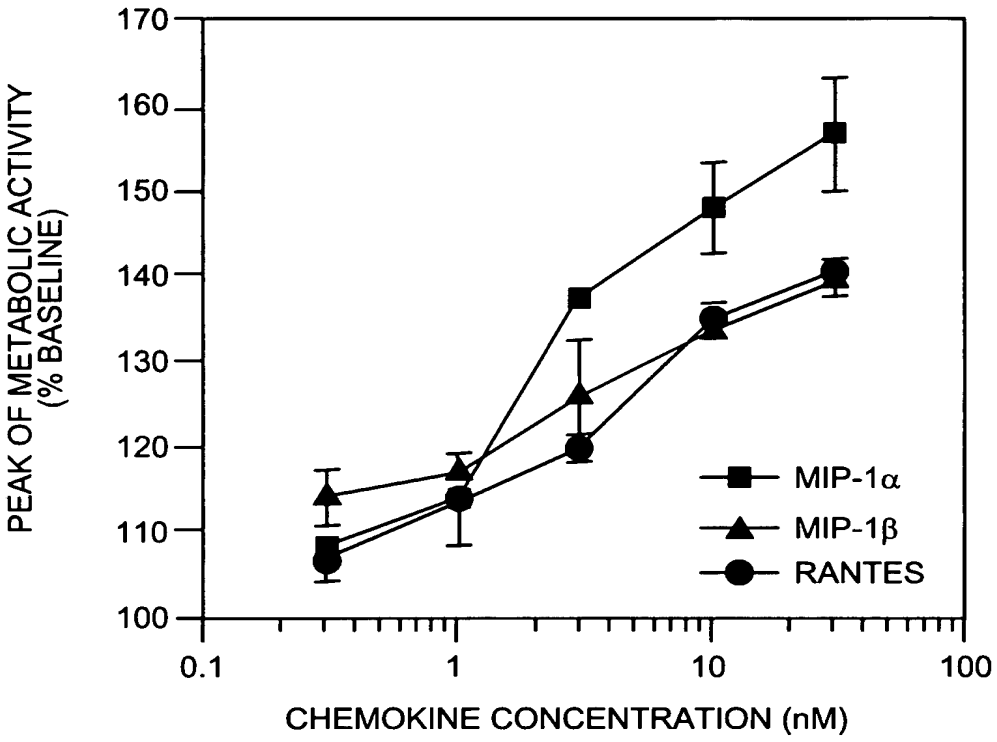

170
160
150
140
130
120
110
100
PEAK OF METABOLIC ACTIVITY
(% BASELINE)
0.1
1
10
100
CHEMOKINE CONCENTRATION (nM)
MIP-1α
MIP-1β
RANTES

FIG. 4C

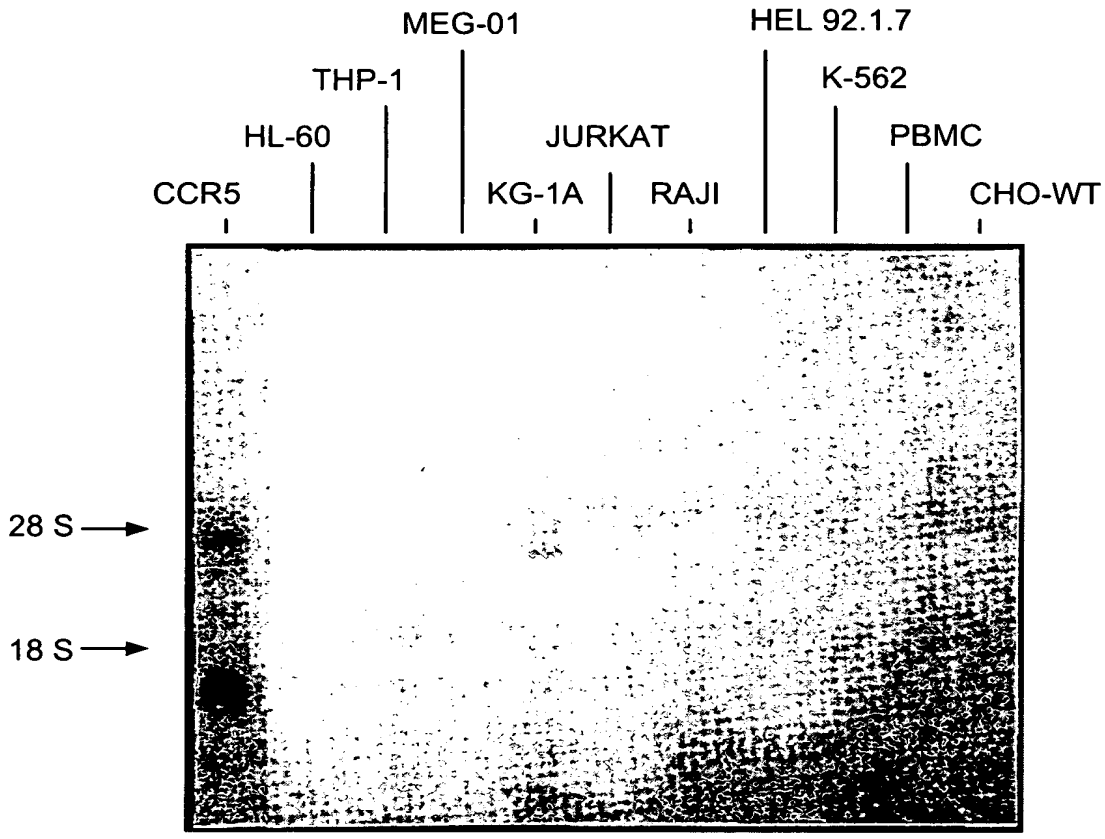

MEG-01
HEL 92.1.7
THP-1
K-562
HL-60
JURKAT
PBMC
CCR5
KG-1A
RAJI
CHO-WT
28 S
18 S

FIG. 5

FIG. 6A
FIG.6B

FIG. 6

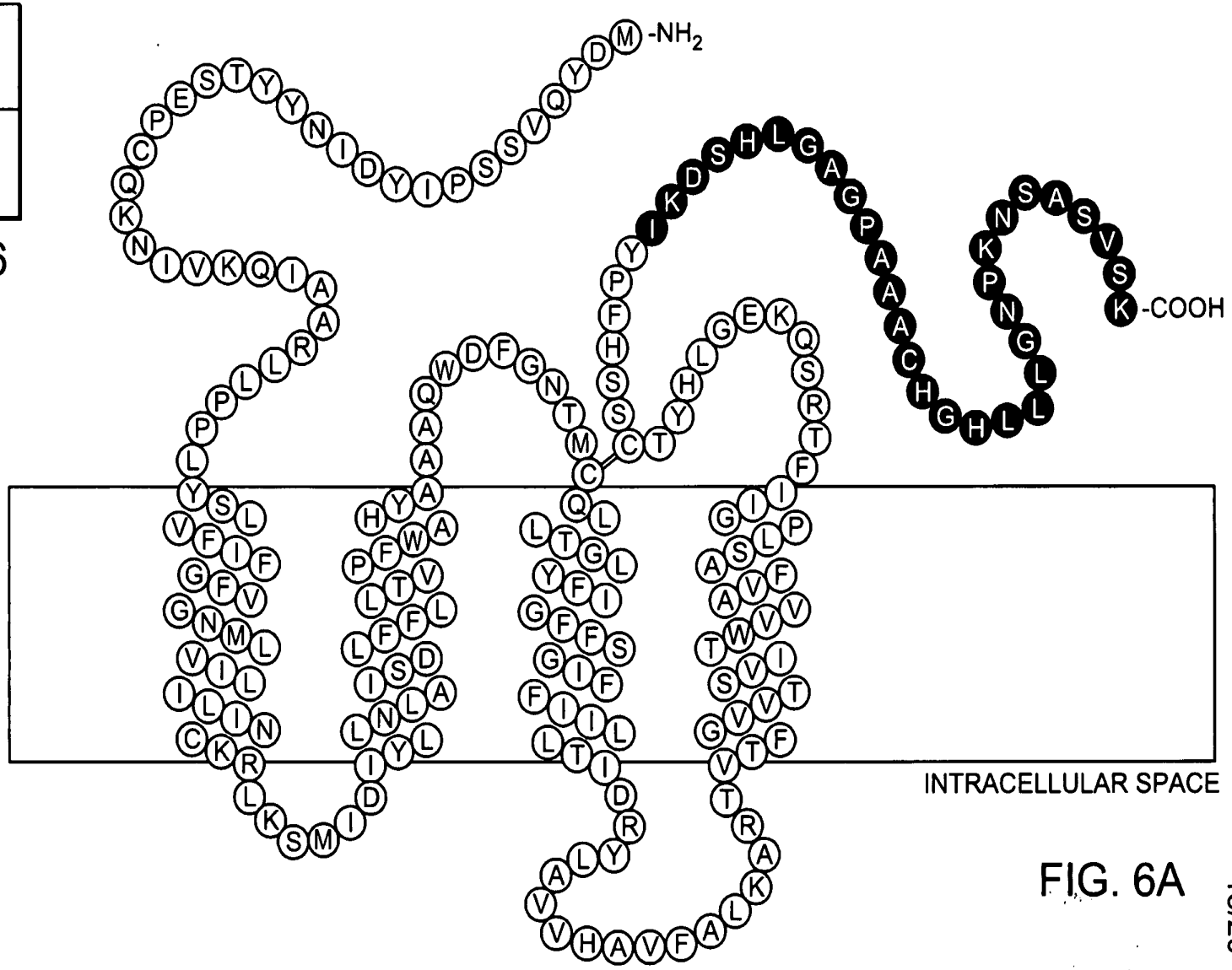


FIG. 6A

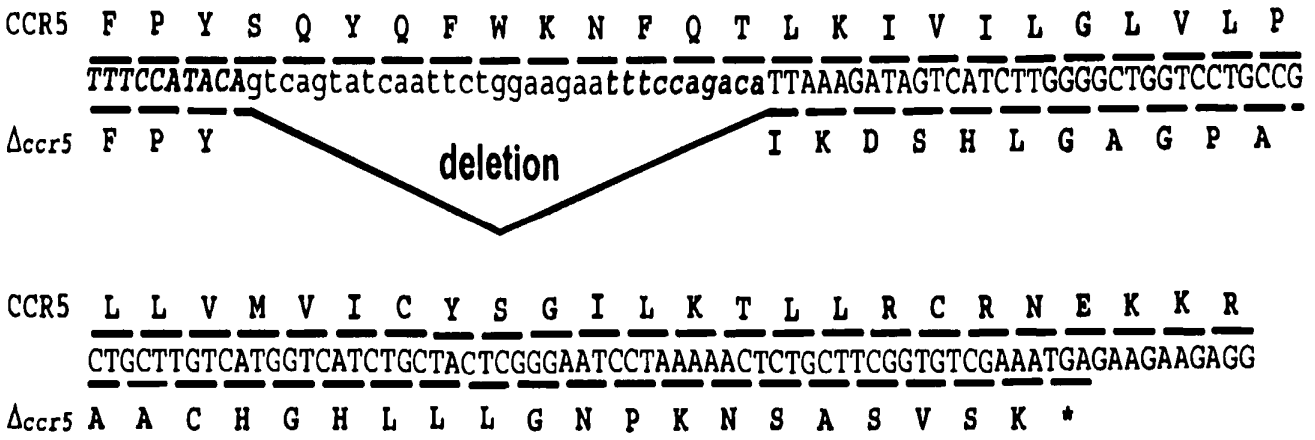

CCR5 F P Y S Q Y Q F W K N F Q T L K I V I L G L V L P
TTTCCATACAgtcagtatcaattctggaagaatttccagacaTTAAAGATAGTCATCTTGGGGCTGGTCCTGCCG
Δccr5 F P Y
deletion
I K D S H L G A G P A
CCR5 L L V M V I C Y S G I L K T L L R C R N E K K R
CTGCTTGTCATGGTCATCTGCTACTCGGGAATCCTAAAAACTCTGCTTCGGTGTCGAAATGAGAAGAAGAGG
Δccr5 A A C H G H L L L G N P K N S A S V S K *

FIG. 6B

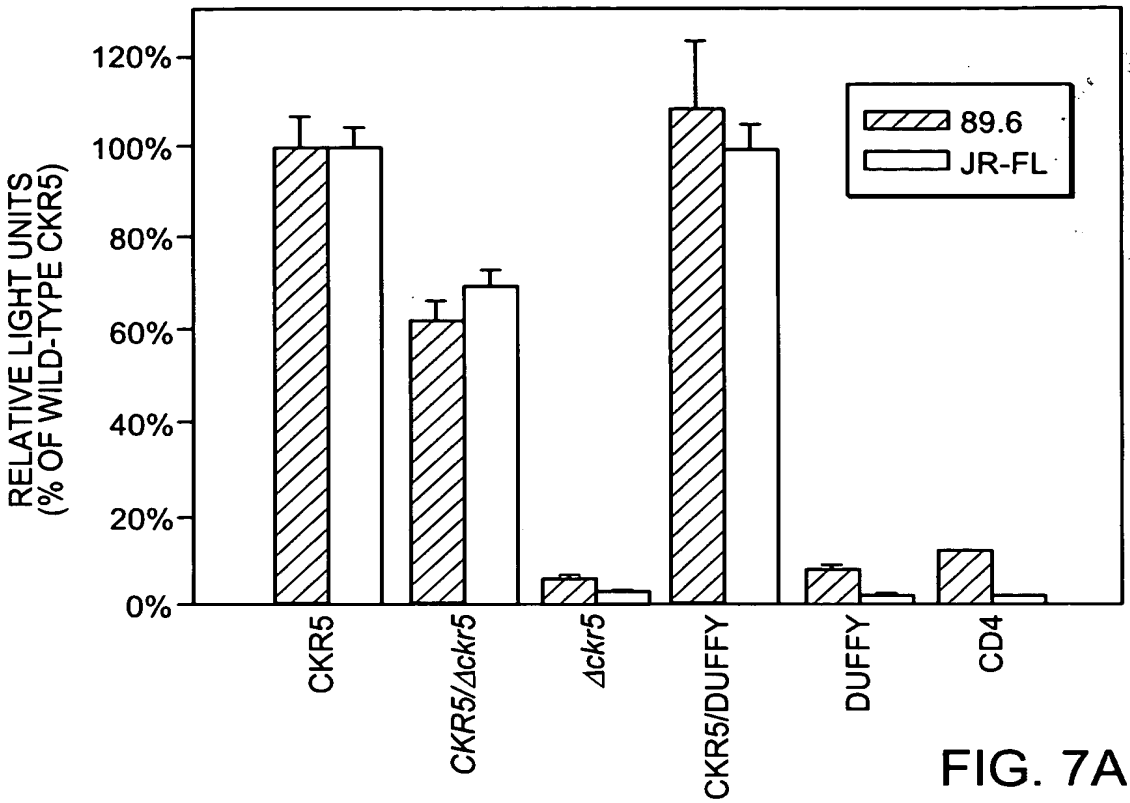

RELATIVE LIGHT UNITS
(% OF WILD-TYPE CKR5)
120%
100%
80%
60%
40%
20%
0%
89.6
JR-FL
CKR5
CKR5/Δckr5
Δckr5
CKR5/DUFFY
DUFFY
CD4

FIG. 7A

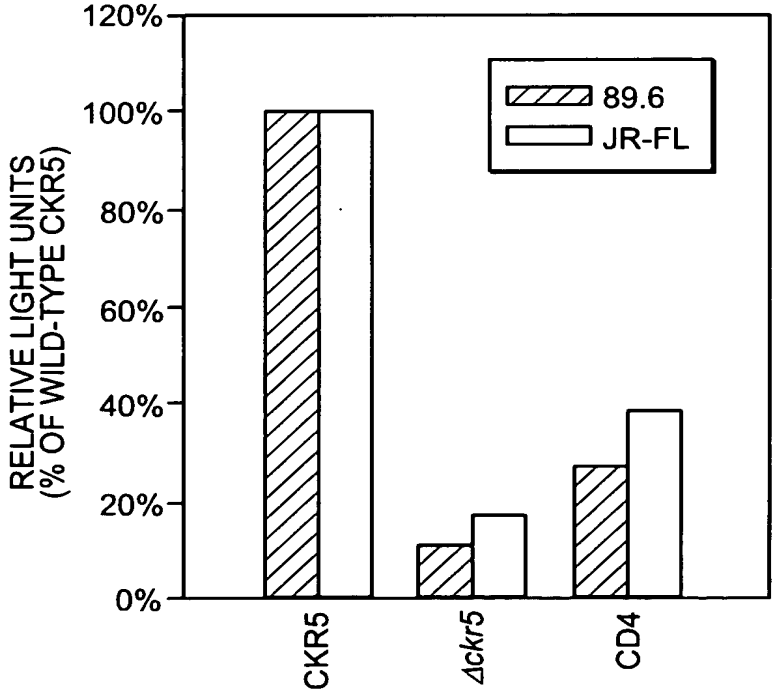

RELATIVE LIGHT UNITS
(% OF WILD-TYPE CKR5)
120%
100%
80%
60%
40%
20%
0%
89.6
JR-FL
CKR5
Δckr5
CD4

FIG. 7B

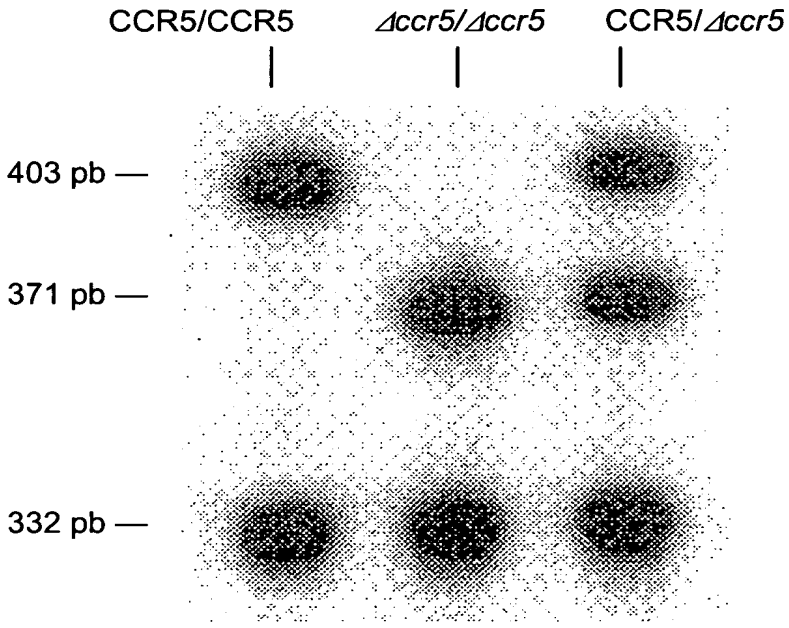
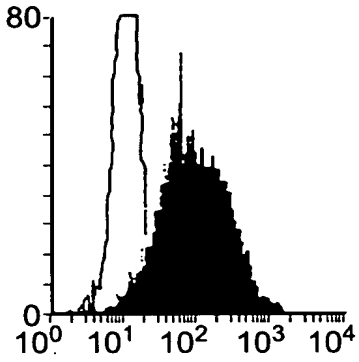
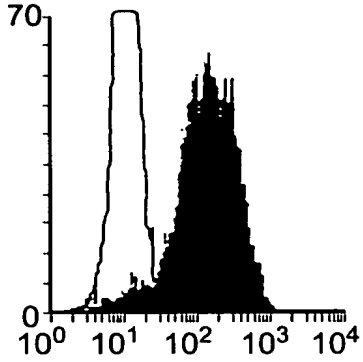


FIG. 8



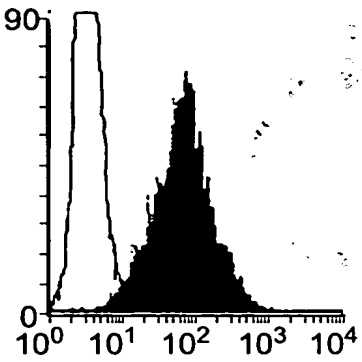
A0

FIG. 9A



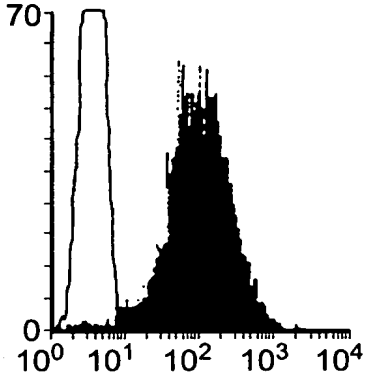
A1

FIG. 9B



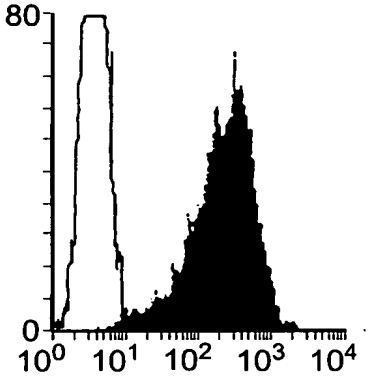
A2

FIG. 9C



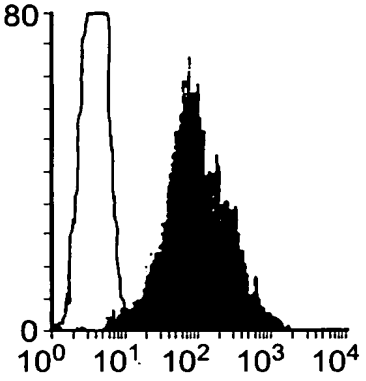
A5

FIG. 9D



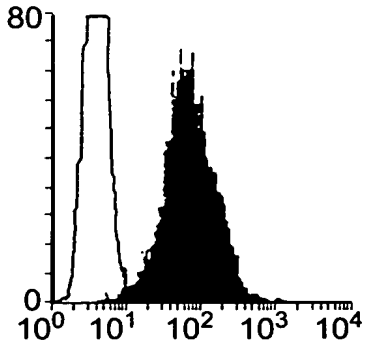
A4

FIG. 9E



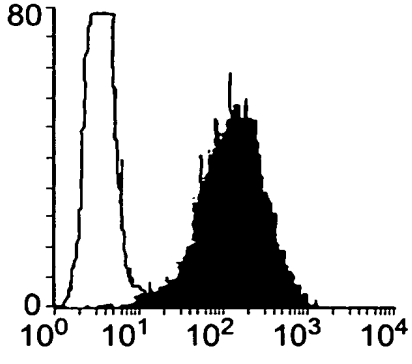
B0

FIG. 9F



B1

FIG. 9G



B3

FIG. 9H

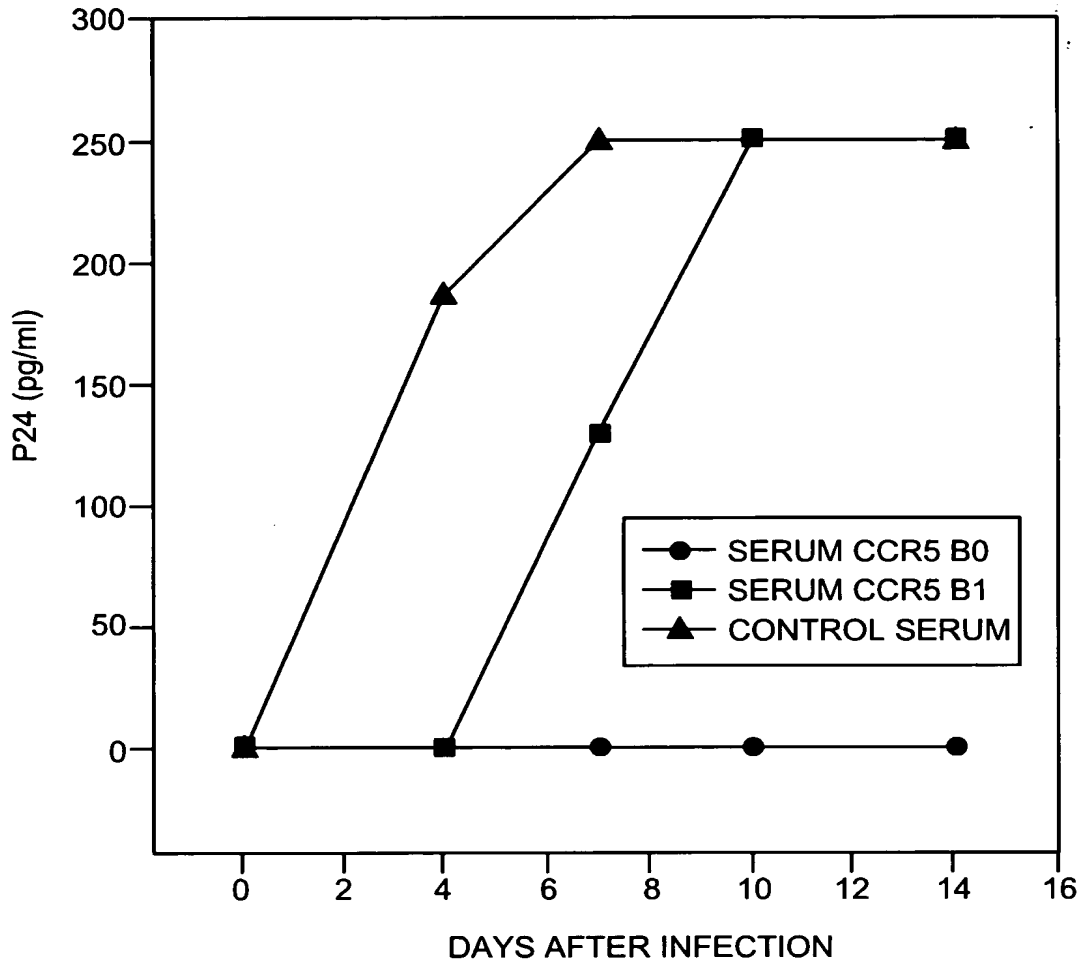

300
250
200
150
100
50
0
P24 (pg/ml)
0
2
4
6
8
10
12
14
16
DAYS AFTER INFECTION
SERUM CCR5 B0
SERUM CCR5 B1
CONTROL SERUM

FIG. 10